

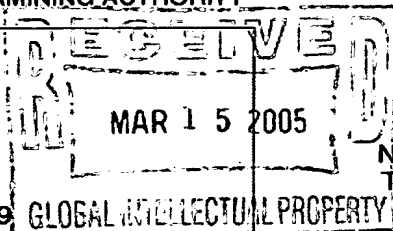
PATENT COOPERATION TREATY

4/11/05

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

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PCT

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Rule 71.1)

Date of mailing (day/month/year) 08.03.2005	
Applicant's or agent's file reference PU5020WO	IMPORTANT NOTIFICATION
International application No. PCT/US 03/39732	International filing date (day/month/year) 12.12.2003
	Priority date (day/month/year) 13.12.2002
Applicant SMITHKLINE BEECHAM CORPORATION et al.	



1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.
2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.
3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.
4. **REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

The applicant's attention is drawn to Article 33(5), which provides that the criteria of novelty, inventive step and industrial applicability described in Article 33(2) to (4) merely serve the purposes of international preliminary examination and that "any Contracting State may apply additional or different criteria for the purposes of deciding whether, in that State, the claimed inventions is patentable or not" (see also Article 27(5)). Such additional criteria may relate, for example, to exemptions from patentability, requirements for enabling disclosure, clarity and support for the claims.



Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Hebert, W Tel. +49 89 2399-2152	
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PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference PU5020WO	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/PEA416)	
International application No. PCT/US 03/9732	International filing date (day/month/year) 12.12.2003	Priority date (day/month/year) 13.12.2002
International Patent Classification (IPC) or both national classification and IPC A61K31/46, A61K31/438, A61P31/18, A61P31/04, C07D451/02, C07D471/10, C07D333/52, C07D211/26, C07D401/04		
Applicant SMITHKLINE BEECHAM CORPORATION et al.		
<p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 7 sheets, including this cover sheet.</p> <p><input type="checkbox"/> This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of sheets.</p>		
<p>3. This report contains indications relating to the following items:</p> <ul style="list-style-type: none"> I <input checked="" type="checkbox"/> Basis of the opinion II <input type="checkbox"/> Priority III <input checked="" type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicability IV <input checked="" type="checkbox"/> Lack of unity of invention V <input checked="" type="checkbox"/> Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement VI <input type="checkbox"/> Certain documents cited VII <input type="checkbox"/> Certain defects in the international application VIII <input type="checkbox"/> Certain observations on the international application 		
Date of submission of the demand 17.06.2004	Date of completion of this report 08.03.2005	
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Härtinger, S Telephone No. +49 89 2399-8289 	

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. **PCT/US 03/39732**

I. Basis of the report

1. With regard to the elements of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

Description, Pages

1-76 as originally filed

Claims, Numbers

1-39 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
☐ the language of publication of the international application (under Rule 48.3(b)).
☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
☐ filed together with the international application in computer readable form.
☐ furnished subsequently to this Authority in written form.
☐ furnished subsequently to this Authority in computer readable form.
☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
☐ the claims, Nos.:
☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. **PCT/US 03/39732**

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 23-27,37-39

because:

☒ the said international application, or the said claims Nos. 23-27,37-39 with respect to IA relate to the following subject matter which does not require an international preliminary examination (specify):

see separate sheet

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the said claims Nos.

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the Standard.

☐ the computer readable form has not been furnished or does not comply with the Standard.

IV. Lack of unity of invention

1. In response to the invitation to restrict or pay additional fees, the applicant has:

☐ restricted the claims.

☒ paid additional fees.

☐ paid additional fees under protest.

☐ neither restricted nor paid additional fees.

2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is

☐ complied with.

☒ not complied with for the following reasons:

see separate sheet

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. **PCT/US 03/39732**

4. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this report:

- ☐ all parts.
- ☒ the parts relating to claims Nos. 1-39(part) .

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	
	No: Claims	1-39
Inventive step (IS)	Yes: Claims	
	No: Claims	1-39
Industrial applicability (IA)	Yes: Claims	1-22,28-36
	No: Claims	

2. Citations and explanations

see separate sheet

Section III:

1. Claims 23-27 and claims 37-39 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Art. 34(4)(a)(I) PCT).
2. As indicated in the annex to the International search report (ISR), a vast number of novelty destroying compounds were retrieved in the initial phase of search for the compound claims. The scope of the search had therefore to be limited. Care should thus be taken when reading this report that certain subject-matter could not be searched.
3. Further to the invitation to pay additional search fees, only one fee was paid for the search of below indicated Group D. Thus with the payment of further examination fees, this report could only be established for the searched subject-matter relating to below Groups A and D (Rule 66.1 e) PCT).

Section IV:

1. For the reasons indicated in the annex to the ISR, the claimed matter does not comply with the requirement of unity of invention (Rule 13.1 PCT). Basically, the combination of ring A with a cyclohexyl containing moiety is already known in the field of antiviral and/or antibacterial agents. Consequently, those features, which are common to all variants claimed, cannot serve as a "special technical feature" in the sense of Rule 13.2 PCT, such that the following groups of inventions have been found, which are not so linked as to for a single inventive concept.

Group A: ring A is an aromatic bicyclic ring

Group B: ring A is an aromatic monocycle

Group C: ring A is a saturated monocycle

Group D: ring A is a saturated bicycle

Section V:

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/US 03/39732

1. The relevant prior art for the subject-matter searched is represented by the following documents (indication of ISR used).

D1: EP-A-1182195; D2: WO-A-0172751; D3: EP-A-1403255;
D4: US-A-6479487; D5: WO-A-0049018; D6: XP002282653;
D7: WO-A-9720823; D8: DE-A-4417163; D9: WO-A-9959974;
D10: WO-A-9964044; D11: WO-A-9709308; D12: WO-A-03087098;
D13: WO-A-03068237; D14: WO-A-03070244; D15: WO-A-03075853;
D16: WO-A-03028641;
D17: BIOORG. MED. CHEM. LET., 11, 2001, 2177-2180 & XP002208447;
D19: WO-A-0190106; D20: WO-A-0218335; D18: WO-A-02074770;
D21: EP-A-1236726; D22: WO-A-9825897; D23: WO-A-0136418.

Those documents which have been cited under the categories "E" or "P,X" in the ISR do not represent prior art as defined by the PCT. However, these documents will become relevant to the issue of novelty in the regional phase before the EPO.

2. Group A invention

The application does not meet the novelty and inventive step requirements of Art. 33(2) and (3) PCT. The novelty destroying passages in the prior art are indicated in the ISR.

As to the inventive step, the problem underlying the present application is considered to represent the provision of further antiviral and/or antibacterial agents. Given the fact that novelty destroying compounds are known, which share this medical utility, the skilled person would not have doubt that compounds having the invariable structural parts of Group A, ie. a 1,4-disubstituted cyclohexyl ring, wherein one substituent comprises a nitrogen atom containing group R1 and wherein the other substituent is a nitrogen containing ring being linked through a linker X, exhibit the desired activity. In the light of the breadth of the present claims, it is therefore not clear which structural feature (or combination of features) could justify the presence of inventive step.

3. Group D invention

The application does not meet the novelty and inventive step requirements of Art.

33(2) and (3) PCT. The novelty destroying passages in the prior art are indicated in the ISR for documents D17, D22 and D23.

With regard to D18, D20 and D21 a selection of the present para substituted cyclohexyl ring has been made. As this structural fragment has not been individualised in these prior art documents, novelty appears to be preset with regard to these documents. As to D19, novelty resides from the present amino containing group R1.

The technical problem underlying the present application is considered to represent the provision of further antiviral and/or antibacterial agents. Given the fact that novelty destroying compounds are known, which share this medical utility, the skilled person would also not have doubt that compounds having the invariable structural parts of Group D, ie. a 1,4-disubstituted cyclohexyl ring, wherein one substituent comprises a nitrogen atom containing group R1 and wherein the other substituent is a nitrogen containing polycyclic hetero ring being linked through a linker X, exhibit the desired activity. With regard to the proposed breadth of the claim, it is therefore not clear which structural feature (or combination of features) could make the not obvious contribution for essentially all variants claimed to the prior art, since the applicant himself considers any of the terminal portions of the molecule, which are assumed to interact with the chemokine receptor, to be variable. Inventive step in the sense of Art. 33(3) PCT is therefore not considered to be met.